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EXAMINER				
KUBELIK, ANNE R				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/520,204

Applicant(s)

DANIELL, HENRY

Examiner

Anne R. Kubelik

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2007 and 28 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11-14, 17 and 20-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-14, 17 and 20-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 1-9, 11-14, 17 and 20-36 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The drawings filed 28 January 2008 are objected to because no details can be made out in Fig 1B and Fig 9, and the lettering is difficult to make out in Fig 1A.
4. The title of the invention is not descriptive of the instantly claimed invention, which is a plastid transformation vector encoding merA and merB. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.
5. The abstract is not descriptive of the instantly claimed invention, as above. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.
6. The objection to claims 2, 6, 14, 25, 29 and 34-35 because informalities is withdrawn in light of Applicant's amendment to the claims.
7. The rejection of claim 37 under 35 U.S.C. 102(b) as being anticipated by Daniell (WO 99/10513) is obviated by Applicant's cancellation of the claim.
8. The rejection of claims 1-9, 11-15 and 18-37 under 35 U.S.C. 102(a) as being anticipated by Daniell et al (WO 01/64024) is withdrawn in light of Applicant's amendment to the claims.

9. The rejection of claims 1-16 and 18-37 under 35 U.S.C. 103(a) as being unpatentable over Daniell (WO 99/10513) in view of Meagher et al (1999, US Patent 5,965,796) is withdrawn in light of Applicant's amendment to the claims.

Claim Objections

1. Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. The objection is repeated for the reasons of record as set forth in the Office action mailed 23 March 2007. Applicant's arguments filed 24 September 2007 have been fully considered but they are not persuasive.

Applicant urges that the objection is overcome by amendment (response pg 9).

This is not found persuasive because plastid genomes are not different when they are in one type of plastid than another. Thus, the claim fails to further limit claim 1. The fails to recite a structure that is different in the vector of claim 9.

10. Claim 31 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. As aadA is not an antibiotic free- selectable marker, as required by claim 29, claim 31 is broader than claims 29-30.

Claim Rejections - 35 USC § 112

2. Claims 13, 21 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that

Applicant regards as the invention. Dependent claims are included in all rejections. Due to Applicant's amendment of the claims, the rejection is modified from the rejection set forth in the Office action mailed 23 March 2007, as applied to claims 1-25 and 34-40. Applicant's arguments filed 24 September 2007 have been fully considered but they are not persuasive.

Claim 36, line 1, is indefinite in its recitation of "including". It is unclear of the plastid comprises the DNA or expression cassette or if the plant cell comprises a plastid and the DNA or expression cassette.

Applicant urges that rejection is overcome by amendment (response pg 9).

This is not found persuasive because this portion of the claim was not amended.

The following rejections are new, due to Applicant's amendment of the claims:

If in claim 13, Applicant is claiming the vector in a plant, the claim should be rewritten to claim a plant transformed by the vector. If, however, Applicant is describing a feature of the vector, the claim needs substantial amendment.

Claim 21 lacks antecedent basis for the limitation "said at least one ...compound".

Claim Rejections - 35 USC § 103

3. Claims 1-9, 11-14, 17 and 20-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniell et al (WO 01/64024) in view of Rathinasabapathi et al (1994, *Planta* 193:155-162). The rejection is repeated for the reasons of record as set forth in the Office action mailed 23 March 2007, as applied to claims 1-37. Applicant's arguments filed 24 September 2007 have been fully considered but they are not persuasive.

The claims are drawn to plastid transformation vectors encoding *merA*, *merB* and *BADH*.

Daniell et al teach a plastid transformation vector comprising a first flanking sequence (*trnI*), a promoter (16S *Prn*), a selectable marker (*aadA*), sequences encoding *MerA* and *MerB* arranged as an operon, a terminator (3' *psbA*), and a second flanking sequence (*trnA*) (Figs 8 and 12-13;), tobacco, *Chlorella* and *Synechocystis* thereby transformed, as well and progeny and seeds from the tobacco plants, and a method comprising exposing the plants to mercury (Figs 9-11; pg 30, line 2, to pg 35, line 9). The flanking sequences would be "conserved in the plastid genome of a plant species" and are from a transcriptionally active region. Daniell et al do not disclose *BADH* as the selectable marker.

Rathinasabapathi et al teach transformation of tobacco plants with a spinach or beet gene encoding *BADH* (pg 157). The protein is targeted to the chloroplasts (pg 157-158) and the resulting plants are resistant to betaine aldehyde (pg 159-160).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the plastid transformation vectors taught by Daniell et al, to use the *BADH* gene as a selectable marker as described in Rathinasabapathi et al. One of ordinary skill in the art would have been motivated to do so because of the suggestion of Rathinasabapathi et al to use betaine aldehyde resistance as a selectable marker in plants that lack glycine betaine (paragraph spanning the columns, pg 161) and because substitution of chloroplast transformation for chloroplast targeting of a nuclear-encoded gene is an obvious design choice.

Applicant urges that Rathinasabapathi et al do not know *BADH*'s location in the chloroplast, And Applicant proposes it may on the outside surface (response pg 10).

This is not found persuasive because Rathinasabapathi et al found transformed BADH in the stroma and not associated with chloroplast membranes (pg 158, right column, paragraph 1); their statement that intermembrane location could not be excluded is their merely hedging their bets. Their data teach a stromal location.

Applicant urges that Rathinasabapathi et al teach that the growth of the transformed plants is retarded, and Applicant suggests this is due to the interaction of betaine aldehyde with the cytoplasm (response pg 10-11).

This is not found persuasive because Rathinasabapathi et al suggests using betaine aldehyde resistance as a selectable marker in plants that lack glycine betaine (paragraph spanning the columns, pg 161). Thus, Rathinasabapathi et al does not consider the retarded growth an insurmountable problem for this use. Further, transformed plants are not exposed to selection media for their entire lives; once transformation is established, selection pressure is eased and plants are grown for the other gene(s) that were transformed with the selective marker. Thus, retarded growth would be a problem if BADH were used as a selection marker.

Applicant urges that the examiner put an affidavit or declaration on the record that substitution of chloroplast transformation for chloroplast targeting of a nuclear-encoded gene is an obvious design choice (response pg 11).

This is not found persuasive. Given that both methods result in the same result, expression of the protein in the chloroplast, selection of one over the other can only be a design choice.

Applicant urges that the combined references do not produce all the features of the claimed invention (response pg 11).

This is not found persuasive because applicant fails to point to any features not in the combination of references.

4. Claims 1-9, 11-14, 17 and 20-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniell (WO 99/10513) in view of Meagher et al (1999, US Patent 5,965,796), and further in view of Rathinasabapathi et al (1994, Planta 193:155-162). The rejection is repeated for the reasons of record as set forth in the Office action mailed 23 March 2007, as applied to claim 17. Applicant's arguments filed 24 September 2007 have been fully considered but they are not persuasive.

The claims are drawn to plastid transformation vectors encoding merA and merB with BADH as the selectable marker.

Daniell disclose plastid transformation vectors comprising a first flanking sequence (trnI), a promoter (16S Prmn or PatpB), a selectable marker (aadA or hyg-R), a sequence expressing a second protein (GFP or CryIIA), a terminator (3' psbA), and a second flanking sequence (trnA) (Fig 6-8). Hyg-R is an antibiotic-free selectable marker. trnI and trnA are sequences in a spacer regions and are highly conserved in plant species (pg 20, lines 20-25). Daniell et al disclose plants transformed with the vectors and progeny and seeds of those plants (pg 42, line 10, to pg 51, line 10; pg 57, line 1, to pg 60, line 36).

Daniell et al do not disclose merA and merB in those vectors or use of BADH as the selectable marker.

Meagher et al teach plants expressing both merA and merB (claims 2, 16, 18 and 26).

Rathinasabapathi et al teach transformation of tobacco plants with a spinach or beet gene encoding BADH (pg 157). The protein is targeted to the chloroplasts (pg 157-158) and the

resulting plants are resistant to betaine aldehyde (pg 159-160).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the plastid transformation vectors taught by Daniell in view of Meagher et al, to use the BADH gene as a selectable marker as described in Rathinasabapathi et al and the express the merA and merB genes described in Meagher et al. One of ordinary skill in the art would have been motivated to do the latter because expression as an operon in the plastid would allow production of stoichiometric amounts of the two enzymes in the pathway. One of ordinary skill in the art would have been motivated to do the former because of the suggestion of Rathinasabapathi et al to use betaine aldehyde resistance as a selectable marker in plants that lack glycine betaine (paragraph spanning the columns, pg 161) and because substitution of chloroplast transformation for chloroplast targeting of a nuclear-encoded gene is an obvious design choice

Applicant urges that Meagher et al did not appreciate the advantage of expressing merA and merB as an operon; thus, one of even extraordinary skill in the art did not recognize this advantage (response pg 12-13).

This is not found persuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, Meagher et al teach the advantages of expressing both proteins (column 12, lines 22-67); expression of both in the plastid would achieve this result.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne Kubelik, Ph.D.
March 16, 2008

/Anne R. Kubelik/
Primary Examiner, Art Unit 1638